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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/775,869	02/10/2004	Ekaterina Dadachova	96700/845	1864

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EXAMINER	
FETTEROLF, BRANDON J	

ART UNIT	PAPER NUMBER
1642	

DATE MAILED: 02/28/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/775,869	DADACHOVA ET AL.	
	Examiner	Art Unit	
	Brandon J. Fetterolf, PhD	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *08 December 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-19,24-33 and 35-37* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-19, 24-33 and 35-37* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

The Election filed on December 8, 2005 in response to the Restriction Requirement of November 30, 2005 has been entered. Applicant's election of Group I, claims 1-19, 24-33 and 35-37, as specifically drawn to a method of treating and/or imaging a tumor in a subject comprising administering an amount of a radiolabeled antibody effective to treat and/or image said tumor has been acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

The restriction requirement is therefore deemed to be proper and is made FINAL.

Claims 1-19, 24-33 and 35-37 are currently pending and under consideration.

Priority

Applicant's claim for domestic priority under 35 U.S.C. 119(e) is acknowledged. After reviewing the Provisional Application, SN: 60/446,684 filed on 02/11/2003, for the disclosure of the genus of cellular components released from a dying cell, the Examiner has established a priority date of **02/10/2004** for claims 1-2 and 3 in part. In the instant case, Provisional Application, SN: 60/446,684 appears to be solely drawn to a single species, i.e., a radiolabeled anti-melanin antibody. As such, the disclosure of a single species in the prior application does not reasonably convey that Applicant's, at the time of the Provisional Application was filed, were in possession of the genus. See Tronzo v. Biomet, 156 F.3d 1154, 1159, 47 USPQ2d 1829, 1833 (Fed. Cir. 1998) (the disclosure of a species in the parent application did not suffice to provide written description support for the genus in the child application.) If applicant disagrees with any rejection of claims 1-2 and 3 set forth in this office action based on examiner's establishment of a priority date of **February 10, 2004** for the instant claims in application serial number 10/775,869 applicant is invited to submit evidence

pointing to the serial number, page and line where support can be found establishing an earlier priority date.

Information Disclosure Statement

The Information Disclosure Statements filed on 4/16/2004, 08/10/2005 and 11/02/2005 are acknowledged. The submission is in compliance with the provisions of 37 CFR 1.97. Accordingly, the information disclosure statement is being considered by the examiner. A signed copy of the IDS is attached hereto.

The listing of references in the specification is not a proper information disclosure statement. 37 CFR 1.98(b) requires a list of all patents, publications, or other information submitted for consideration by the Office, and MPEP § 609.04(a) states, "the list may not be incorporated into the specification but must be submitted in a separate paper." Therefore, unless the references have been cited by the examiner on form PTO-892, they have not been considered.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-3 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. In the instant case, the claims are inclusive of a genus of radiolabeled antibodies which bind to a cellular component released by a dying tumor cell, wherein the cellular component may be a subgenus histones, mitochondrial proteins, cytoplasmic proteins or pigments. Therefore, the claims encompass a genus of molecules defined solely by its principal biological property, which is simply a wish to know the identity of any material with that biological property.

The Written Description Guidelines for examination of patent applications indicates, "the written description requirement for a claimed genus may be satisfied through sufficient description

of a representative number of species by actual reduction to practice, or by disclosure of relevant, identifying characteristics, i.e., structure or other physical characteristics and/or other chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show applicant was in possession of the claimed genus." (Federal register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001, see especially page 1106 column 3) and (see MPEP 2164).

The specification teaches (page 5, paragraph 0024) that cellular components released from a dying cell include, but are not limited to, a histone, a mitochondrial protein, a cytoplasmic protein, or a pigment. With regards to the histone, the specification teaches (page 5, paragraph 0024) that histones can be one of the major subtypes of histones such as H1, H2A, H2B, H3 and H4. With regards to the pigment, the specification provides (page 5, paragraph 0024) a specific example of a pigment, wherein the pigment is melanin. Thus, while specification provides a specific species of pigment, e.g., melanin, and five further subtypes of histones, the specification does not appear to reasonably convey a representative number of histones, mitochondrial proteins, cytoplasmic proteins or pigments to suggest that they were in possession of the claimed genus and/or subgenus as presently claimed. A description of a genus may be achieved by means of a recitation of a representative number of species falling within the scope of the genus or by describing structural features common the genus that "constitute a substantial portion of the genus." See University of California v. Eli Lilly and Co., 119 F.3d 1559, 1568, 43 USPQ2d 1398, 1406 (Fed. Cir. 1997): "A description of a genus of cDNAs may be achieved by means of a recitation of a representative number of cNDA, defined by nucleotide sequence, falling within the scope of the genus or of a recitation of structural features common to the members of the genus, which features constitute a substantial portion of the genus." The Federal Circuit has recently clarified that a DNA molecule can be adequately described without disclosing its complete structure. See Enzo Biochem, Inc. V. Gen-Probe Inc., 296 F.3d 1316, 63 USPQ2d 1609 (Fed. Cir. 2002). The Enzo court adopted the standard that the written description requirement can be met by "show[ing] that an invention is complete by disclosure of sufficiently detailed, relevant identifying characteristics ....i.e., complete or partial structure, other physical and/or chemical properties, functional characteristics when coupled with a known or disclosed correlation between function and structure, or some combination of such characteristics. " Id. At 1324, 63 USPQ2d at 1613 (emphasis omitted, bracketed material in original).

The court has since clarified that this standard applies to compounds other than cDNAs. See University of Rochester v. G.D. Searle & Co., Inc., __F.3d__,2004 WL 260813, at *9 (Fed.Cir.Feb. 13, 2004). The instant specification fails to provide sufficient descriptive information, such as definitive structural or functional features that are common to the genus. That is, the specification provides neither a representative number of cellular components that encompass the genus of nor does it provide a description of structural features that are common to the genus. Further, the specification fails to provide a representative number of histones, mitochondrial proteins, cytoplasmic proteins or pigments that encompass the genus of cellular components along with a description of structural features that are common to the genus. Since the disclosure fails to describe the common attributes or characteristics that identify members of the genus, and because the genus is highly variant, the disclosure is insufficient to describe the genus. Thus, one of skill in the art would reasonably conclude that the disclosure fails to provide a representative number of species to describe and enable the genus as broadly claimed.

Vas-Cath Inc. v. Mahurkar, 19USPQ2d 1111, clearly states "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention.* The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed.*" (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See *Vas-Cath* at page 1116). As discussed above, the skilled artisan cannot envision the detailed chemical structure(s) of the encompassed genus of cellular components, and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. A lack of adequate written description issue also arises if the knowledge and level of skill in the art would not permit one skilled in the art to immediately envisage the product claimed from the disclosed process. See, e.g., *Fujikawa v. Wattanasin*, 93 F.3d 1559, 1571, 39 USPQ2d 1895, 1905 (Fed. Cir. 1996) Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of isolating it. The compound itself is required. See *Fiers v. Revel*, 25 USPQ2d 1601 at 1606 (CAFC 1993) and *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016.

One cannot describe what one has not conceived. See *Fiddes v. Baird*, 30 USPQ2d 1481 at 1483. In *Fiddes*, claims directed to mammalian FGF's were found to be unpatentable due to lack of written description for that broad class. The specification provided only the bovine sequence.

Therefore, only one species of cellular components, wherein the cellular component is melanin, but not the full breadth of the claims, meets the written description provision of 35 U.S.C. §112, first paragraph. Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 U.S.C. §112 is severable from its enablement provision (see page 1115).

Claims 1-19, 25-33 and 35-37 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of treating and/or imaging a tumor comprising administering a radiolabeled antibody which binds to a histone, mitochondrial protein or cytoplasmic protein and a method of treating and/or imaging melanin containing melanoma in a subject comprising administering an amount of a radiolabeled antimelanin antibody, wherein the antimelanin antibody is 6D2, does not reasonably provide enablement for a method of treating and/or imaging any and/or all tumors, including melanoma, comprising administering any and/or all radiolabeled antibodies specific for melanin. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

The factors to be considered in determining whether undue experimentation is required are summarized In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988). The court in Wands states: "Enablement is not precluded by the necessity for some experimentation such as routine screening. However, experimentation needed to practice the invention must not be undue experimentation. The key word is 'undue,' not 'experimentation.' " (Wands, 8 USPQ2d 1404). Clearly, enablement of a claimed invention cannot be predicated on the basis of quantity of experimentation required to make or use the invention. "Whether undue experimentation is needed is not a single, simple factual determination, but rather is a conclusion reached by weighing many factual considerations." (Wands, 8 USPQ2d 1404). The factors to be considered in determining whether undue experimentation is required include: (1) the quantity of experimentation necessary, (2) the amount or direction or guidance presented, (3) the presence or absence of working examples,

(4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims.

Claims 1-4 read on a method of treating and/or imaging a tumor comprising administering a radiolabeled antibody specific for a cellular component released from a dying tumor cell including, but not limited to, melanin. Thus, claims 1-4 read a method of treating and/or imaging any and/or all tumors comprising administering any and/or all radiolabeled antibodies specific for a cellular component including, but not limited to, melanin. Claims 5-19, 25-33 and 35-37 read on a method of treating and/or imaging a melanin-containing melanoma comprising administering a radiolabeled antimelanin antibody. Thus, the claims read on administration of any and/or all radiolabeled antimelanin antibodies.

The scope of the instant claims is not commensurate with the enablement of the instant disclosure, because practice of the claimed invention would require undue experimentation by an artisan of ordinary skill in the art. The instant specification is not enabling for claims drawn to a method of treating and/or imaging any and/or all tumors, including melanoma comprising administering any and/or all radiolabeled antibodies specific for melanin. The specification teaches (page 5, paragraph 0024) that the present invention involves a method of treating and/or imaging tumors in a subject comprising administering a radiolabeled antibody effective to treat or image the tumor, wherein the antibody binds to a cellular component released by a dying tumor cell including, but not limited to, a histone, a mitochondrial protein, a cytoplasmic protein or a pigment, e.g., melanin. With regards to the tumor, the specification teaches (page 6, paragraph 0030) that the term "tumor" includes melanoma. The specification further provides (page 13, paragraph 0055 to 0056 and page 14, paragraph 0059 to 0060) the in vivo binding/distribution of radiolabeled antimelanin antibody 6D2 in melanoma containing mice, as well as the radioimmunotherapy of melanomas using the radiolabeled antimelanin antibody 6D2. Moreover, the specification provides a prospective example (beginning on page 16, paragraph 0067) on how to make and/or use antibodies to human melanin. Thus, while the specification clearly conveys the treatment and/or imaging of melanin containing melanoma's comprising administering radiolabeled 6D2 anti-melanin antibody, the specification appears to be silent on the treatment of any other tumor or the specificity of any other anti-melanin antibody.

The closest prior art to the instantly claimed invention is Mason et al. (Cancer Research 1954; 14; 648-650), whom teaches a radiolabeled anti-melanin antibody (abstract). Specifically, the reference teaches that that administration of a radiolabeled anti-melanin antibody to mice bearing melanin containing melanoma's resulted in no significant localization of radioactivity, wherein the failure to localize may be ascribed to several causes, most likely of which is the relative impermeability of mouse melanoma cells to rabbit antibodies (page 650, 1st column, 1st paragraph to 2nd paragraph).

As such, the instant specification provides insufficient guidance and objective evidence to predictably enable one of skill in the art to use the invention as claimed. Those of skill in the art would recognize the unpredictability of using any radiolabeled antibody to melanin for radioimmunotherapy and/or radio imaging. For example, Wilder et al. (J. Clin. Oncol. 1996; 14: 1383-1400) discloses challenges that currently face radioimmunotherapy (abstract). These challenges include: (1) circulating free antigen, biding of antibodies to nonspecific Fc receptors, insufficient tumor penetration, antigenic heterogeneity and insufficient antigen expression, antigenic modulation and development of human antimouse antibodies. Wilder et al. further teach the importance of dosimetry for treatment planning and assessment of results, wherein dosimetry is dependent on the kinetics of uptake and clearance of radiolabeled antibodies, the distribution of radiolabeled antibodies and the radioisotope attached to the antibody (page 1387, 1st column, 3rd paragraph from bottom). For example, Wilder et al. teach that the transport of antibodies through the intestinal space of a tumor by diffusion and convection is impeded by antigen binding and relatively large extravascular distances which results in a heterogeneous distribution of antibodies. Along the same lines, Erdi et al. (Phys. Med. Biol. 1996; 41: 2009-20026) disclose that although RIT (radioimmunotherapy) is an innovative and promising approach, there is problems to be solved which limit its use (page 2009, Introduction). These problems include: (1) the low uptake of the radiolabeled antibody; (2) the low target:non-target ratios and the inhomogenous distribution of antibodies within the tumor. While these reference demonstrate the importance of the specificity, uptake and distribution of the antibody in radioimmunotherapy, the same consideration and/or problems associated with RIT are found with radio imaging as well, see for example Chatel et al. (Eur. J. Nucl. Med. 1992; 19: 205-213). As such, in view of the teachings of Mason et al, supra, the skilled artisan would not have found sufficient guidance in the specification to achieve an effective

method of treating an/or imaging tumors comprising administering any and/or all radiolabeled antibodies to melanin.

In view of the lack of guidance and the large amount of experimentation in an unpredictable art, it would require undue experimentation to practice the claimed invention.

Claim 24 is rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention because the specification does not provide evidence that the claimed biological materials are (1) known and readily available to the public; (2) reproducible from the written description.

It is unclear whether a cell line which produces an antibody having the exact chemical identity of 6D2 is known or publicly available, or can be reproducibly isolated without undue experimentation. Therefore, a suitable deposit for patent purposes is suggested. Without a publicly available deposit of the above cell line, one or ordinary skill in the art could not be assured of the ability to practice the claimed invention as claimed. Exact replication of: (1) the claimed cell line; (2) a cell line which produces the chemically and functionally distinct antibody claimed; and/or (3) the claimed antibody's amino acid or nucleic acid sequence is an unpredictable event.

For example, very different V_H chains (about 50% homologous) can combine with the same V_K chain to produce antibody-binding sites with nearly the same size, shape, antigen specificity, and affinity. A similar phenomenon can also occur with very similar properties. The results indicate that divergent variable region sequences, both in and out of the complementarity-determining regions, can be folded to form similar binding site contours, which result in similar immunochemical characteristics. [FUNDAMENTAL IMMUNOLOGY 242 (William E. Paul, M.D. ed., 3rd ed. 1993)]. Therefore, it would require undue experimentation to reproduce the claimed antibody species 6D2. Deposit of the hybridoma would satisfy the enablement requirements of 35 U.S.C. 112, first paragraph. See, 37 C.F.R. 1.801-1.809.

If a deposit is made under the terms of the Budapest Treaty, then an affidavit or declaration by applicants or someone associated with the patent owner who is in a position to make such assurances, or a statement by an attorney of record over his or her signature, stating that the deposit has been made under the terms of the Budapest Treaty and that all restrictions imposed by the

depositor on the availability to the public of the deposited material will be irrevocably removed upon the granting of a patent, would satisfy the deposit requirements. See, 37 CFR 1.808.

If a deposit is not made under the terms of the Budapest Treaty, then an affidavit or declaration by applicants or someone associated with the patent owner who is in a position to make such assurances, or a statement by an attorney of record over his or her signature, stating that the deposit has been made at an acceptable depository and that the following criteria have been met:

(a) during the pendency of this application, access to the invention will be afforded to one determined by the Commissioner to be entitled thereto;
(b) all restrictions imposed by the depositor on the availability to the public of the deposited material will be irrevocably removed upon granting of the patent;
(c) the deposit will be maintained for a term of at least thirty (30) years and at least five (5) years after the most recent request for the furnishing of a sample of the deposited material;
(d) a viability statement in accordance with the provisions of 37 CFR 1.807; and
(e) the deposit will be replaced should it become necessary due to inviability, contamination or loss of capability to function in the manner described in the specification.

Amendment of the specification to recite the date of deposit and the complete name and address of the depository is required. As an addition means for completing the record, applicant may submit a copy of the contract with the depository for deposit and maintenance of each deposit.

If a deposit is made after the effective filing date of the application for patent in the United States, a verified statement is required from a person in a position to corroborate that the biological material described in the specification as filed is the same as that deposited in the depository, stating that the deposited material is identical to the biological material described in the specification and was in the applicant's possession at the time the application was filed.

Applicant's attention is directed to In re Lundack, 773 F.2d. 1216, 227 USPQ 90 (CAFC) and 37 CFR 1.801-1.809 for further information concerning deposit practice.

In addition the identifying information set forth in 37 CFR 1.809(d) should be added to the specification. See 37 CFR 1.803 - 37 CFR 1.809 for additional explanation of these requirements.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claim 2 is rejected under 35 U.S.C. 102(b) as being anticipated by Thorpe et al. (US 6,342,221, 2002).

Thorpe et al. teach (column 35, lines 51-60) antibodies specific to internal cellular components of mammalian malignant cells such as histones which are specifically released from necrotic tumor cells. The patent further teaches (column 36, lines 9-21) that these antibodies may labeled and administered to a patient in order to image the necrotic tissue, wherein a localized concentration of the antibody is indicative of the presence of a tumor. With regards to the label, the patent teaches (column 39, lines 24-38) a number of radioisotopes which the antibody may be labeled with.

Claim 1-3 are rejected under 35 U.S.C. 102(b) as being anticipated by Goldenberg (US 4,460561, 1984, IDS).

Goldenberg teaches (abstract) a method of using radiolabeled antibodies specific to intracellular-tumor associated markers for detection, localization and therapy of tumors. With regards to the intracellular-tumor associated markers, the patent teaches (column 2, lines 46-52) that intracellular tumor-associated markers include, but are not limited to, substances which accumulate with in tumor cells such as in the cytoplasm, nucleus or various organelles or subcellular structure. With regards to the detection, Goldenberg teaches (column 5, lines 12-21) that the antibody may be labeled with gallium-67, technetium-99m, and indium-111 for gamma camera imaging of the tumor.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1 and 3 are rejected under 35 U.S.C. 103(a) as being unpatentable over Thorpe et al. (US 6,342,221, 2002) in further view of Goldenberg (US 4,460561, 1984, IDS).

(Note: This rejection applies to claims 1 and 3, wherein the cellular component released from a dying cell is a histone).

Thorpe et al. teach, as applied to claim 2 above, antibodies specific to internal cellular components of mammalian malignant cells such as histones which are specifically released from necrotic tumor cells (column 35, lines 51-60). The patent further teaches (column 36, lines 9-21) that these antibodies may labeled and administered to a patient in order to image the necrotic tissue, wherein a localized concentration of the antibody is indicative of the presence of a tumor. With regards to the label, the patent teaches (column 39, lines 24-38) a number of radioisotopes which the antibody may be labeled with.

Thorpe et al. does not explicitly teach a method of treating a tumor comprising administering a radiolabeled antibody that is specific for a cellular component released from a dying cell such as a histone.

Goldenberg teaches (abstract) a method of using radiolabeled antibodies specific to intracellular-tumor associated markers for detection, localization and therapy of tumors. Moreover, the patent teaches that the radiolabeled antibodies specific for intracellular-tumor associated antigens satisfies the need for a method of tumor detection and localization which is not confined to the use of antibodies to cell-surface antigens, which does not require repeated injections of background compensating material for a subtraction technique, which is adaptable to both diagnosis an therapy (column 1, lines 62-68).

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to combine the teachings of the references so as to treat a tumor using a radiolabeled antibody specific for a internal cellular component such as histone. One would be motivated to do so because as taught by Goldenberg, radiolabeled antibodies specific for intracellular-tumor associated antigens satisfies the need for a method of tumor detection and localization which is not confined to the use of antibodies to cell-surface antigens, which does not

require repeated injections of background compensating material for a subtraction technique, which is adaptable to both diagnosis an therapy. Thus, one of ordinary skill in the art would have reasonably expectation of success that by administering an antibody specific to a histone as taught by Thorpe et al. that has been radiolabeled in view of Goldberg, one would achieve an effective method of treating tumors via radioimmunotherapy.

Therefore, NO claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Brandon J. Fetterolf, PhD whose telephone number is (571)-272-2919. The examiner can normally be reached on Monday through Friday from 8:30 to 5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeff Siew can be reached on 571-272-0787. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Brandon J Fetterolf, PhD
Examiner
Art Unit 1642

BF

JEFFREY SIEW
SUPERVISORY PATENT EXAMINER
2/13/06